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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,311	04/07/2006	Francis P. Kuhajda	P71522US/37049.00020	5370

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	**PAPER NUMBER**
1627	

MAIL DATE	DELIVERY MODE
12/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,311	KUHAJDA ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *9-11,13-15 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12,16,17,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/18/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 08/18/09. Claims 1-20 are currently pending in the application, with claims 9-11, 13-15, and 18 having being withdrawn. Accordingly, claims 1-8, 12, 16-17, and 19-20 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

Applicant's argument with respect to Kuhajda who does not teach or suggest inhibiting cancer development in pre-cancerous cells has been fully considered. Applicant argues that Kuhajda does not disclose a method of inhibiting cancer development in pre-cancerous cells. Such arguments are not found persuasive as applicant is arguing features not previously found in independent claim 1. It is noted that the features upon which applicant relies (i.e., pre-cancerous cells) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, the Examiner contends that Kuhajda teaches that high levels of fatty acid synthase (FAS) expression exists in a variety of human malignancies and their precursor lesions (i.e. precancerous cells; see pg. 3450, left col., Introduction Section, paragraph 1). Importantly,

Kuhajda et al. teach that the development of C75 now enables extensive in vivo study of FAS inhibition in human cancer (see pg. 3450, right col., Introduction Section, lines 8-11). Kuhajda, however, does not teach treatment of lung cancer using C75. Wang et al., on the other hand, teach expression of FAS in non-small cell lung cancer (i.e. NSCLC, a type of lung cancer; see pg. 1, abstract). Particularly, Wang et al., teach that the survival rate of FAS expression in early lesions (i.e. early cancerous lesions) of NSCLC patients correlated with poor prognosis (see abstract). Consequently, the Examiner contends that one of ordinary skill in the art would have found it obvious to administer and obvious to try C75, the FAS inhibitor, in pre-cancerous lesions (i.e. before the development of cancer given that early lesions of NSCLC result in poor prognosis and given that Kuhajda teaches that FAS is expressed in a variety of human malignancies and precursor lesions. As a result, the Examiner maintains that one of ordinary skill would have been motivated to try C75 in pre-cancerous cells and would have had a reasonable expectation of success since Kuhajda et al. teach its effectiveness against cancer cells. Thus, Kuhajda in view of Wang does indeed render obvious applicant's invention.

While applicant argues that applicant has demonstrated effective treatment with C75 in precancerous cells, the Examiner continues to maintain that such treatment is within the purview of the skilled artisan in light of the teachings of Kuhajda et al. who teach that FAS is involved and play a role in precursor lesions. Consequently, one of ordinary skill in the art would have found it obvious to administer C75 to patients/subjects with pre-cancerous lesions since

Kuhajda teaches that FAS is known to be expressed in precancerous lesions (i.e. pre-cancerous cells) and given that Kuhajda teaches the use of C75 to inhibit FAS expression. As a result, one of ordinary skill in the art would have found it obvious to utilize C75 in pre-cancerous lesions in light of the disclosure of Kuhajda and would have had a reasonable expectation of success since Kuhajda teaches the effective use of C75 in FAS expressing cells and in light of the disclosure of Kuhajda who teaches that FAS expression also occurs in pre-cancerous lesions.

For the foregoing reasons, the rejection of record under 103 (a) remains proper. However, in view of applicant's amendment, the following modified 103 (a) Final rejection is being made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 8, 12, 16-17, and 19-20 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Kuhajda et al. (Kuhajda et al. PNAS March

2000, Vol. 97, Nol. 7, pgs. 3450-3454, previously cited) in view of Wang et al. (Zhonghua Zhong Liu Za Zhi, May 2002, Vol. 24, No. 3, pgs. 271-273, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Kuhajda et al. teach that normal tissues have low levels of fatty acid synthesis while a number of studies have demonstrated high levels of fatty acid synthase (FAS) expression in a wide variety of human malignancies and their precursor lesions (i.e. precancerous cells; see pg. 3450, left col., Introduction Section, paragraph 1). In fact, Kuhajda et al. teach that the widespread expression of FAS in human cancer and its association with aggressive disease suggests that FAS provides an advantage for tumor growth (see left col., Introduction Section, paragraph 2). Thus, in an effort to study the systemic anticancer effects of FAS inhibition *in vivo*, Kuhajda et al. tested a synthetic,

chemically stable inhibitor of mammalian FAS, C75 (i.e. tetrahydro-3-methylene-2-oxo-5-n-octyl-4-furancarboxylic acid; instant claims 1 and 19-20; see pg. 3450, left col., last line and right col., lines 1-2). Specifically, Kuhajda et al. demonstrated that C75 binds to and inhibits mammalian FAS and inhibits fatty acid synthesis in human cancer cells (instant claim 17; see pg. 3450, right col., Introduction Section, lines 4-6). Importantly, Kuhajda et al. teach that the development of C75 now enables extensive *in vivo* study of FAS inhibition in human cancer (see pg. 3450, right col., Introduction Section, lines 8-11). Moreover, Kuhajda et al. teach that C75 was tested in breast cancer xenografts (i.e. *in vivo*) showed significant anti-tumor activity with concomitant inhibition of fatty acid synthesis via direct inhibition with human FAS (instant claim 17; see pg. 3453, left col., Discussion Section, last paragraph and right col.).

Kuhajda et al. do not specifically teach a method inhibiting precancerous lung cancer cells. Similarly, Kuhajda et al. do not teach treatment in humans or dosage administration.

The Examiner however contends that it is well within the purview of the skilled artisan in view of the teachings of Kuhajda et al. to administer C75 to human patients since cancer occurs in human beings. Additionally, it is well within the purview of the skill of the artisan at the time of the invention to adjust the concentration and dosage of C75 for human consumption during the course of routine experimentation so as to obtain the most effective dosage.

While the percentage of C75 is not disclosed by Kuhajda, it is generally noted that differences in concentration or dosages do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of a specific range or dosage of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of ranges is the optimum combination of dosages.

Wang et al. teach expression of FAS in non-small cell lung cancer (i.e. NSCLC, a type of lung cancer; instant claims 8 and 12; see pg. 1, abstract). Particularly, Wang et al. analyzed samples of NSCLC patients and found through immunohistochemical techniques that FAS expression rate was 31.4% with expression highest in non-adenocarcinoma human patients (see abstract). Additionally, Wang et al. teach that the survival rate of FAS expression in early lesions of NSCLC patients correlated with poor prognosis (see abstract).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize and try C75 in pre-cancerous non-small cell lung cancer human patients since Kuhajda teaches studies have demonstrated high

levels of fatty acid synthase (FAS) expression in a wide variety of human malignancies and their precursor lesions and Wang et al. teach that FAS expression was detected NSCLC patients and associated with poor prognosis and in view of the teachings of Kuhajda who teach inhibition of FAS with C75. Moreover, one of ordinary skill in the art would have found it obvious to optimize the dosage administered through routine examination in order to determine the most effective dosages for patients. Thus, given the teachings of Kuhajda and Wang, one of ordinary skill in the art would have been motivated to try and administer C75 in precancerous lung cancer cells with the reasonable expectation of providing a method that is effective in inhibiting cancer development and a method effective in increasing the survival rate of such patients.

Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (Kuhajda et al. PNAS March 2000, Vol. 97, Nol. 7, pgs. 3450-3454, previously cited) in view of Wang et al. (Zhonghua Zhong Liu Az Zhi, May 2002, Vol. 24, No. 3, pgs. 271-273, previously submitted) as applied to claims 1-5, 8, 12, 16-17, and 19-20 above and in further view of Hirsch et al. (British Journal of Cancer, May 2002, Vol. 86, pgs. 1449-1456, previously cited).

The Kuhajda and Wang references are as discussed above and incorporated by reference herein. However, Kuhajda and Wang do not teach that the pre-cancerous lesions express FAS and/or neu protein.

Hirsch et al. teach that the clinical significance of Her-2/neu protein expression in lung cancer is currently under evaluation but certain neu expressing patients show shorter survival (see abstract). Upon investigation of 238 non-small cell lung carcinomas, Hirsch et al. teach that 39 patients express the neu protein wherein 35% of such patients possess adenocarcinomas, 20% large cell carcinomas and 1% squamous cell carcinomas (see abstract). Importantly, Hirsch et al. teach that the findings are consistent with previous reports in the literature of NSCLC patients (see pg. 1453, right col., Discussion Section, last paragraph).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize C75 in non-small cell lung cancer human patients who also express neu protein since Hirsch teaches that NSCLC patients also express the neu protein and can lead to shorter survival. Thus, given the teachings of Kuhajda, Wang, and Hirsch, one of ordinary skill in the art would have been motivated to administer C75 to human lung cancer patients with both neu and FAS expression with the reasonable expectation of providing a method that is effective in inhibiting cancer development and a method effective in increasing the survival rate of such patients.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

12/05/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627